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Clinical Response and Treatment Response in Sputum Positive Diabetic and Non-Diabetic Patients

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Abstract
Tuberculosis is still a major public health problem in the world with an estimated 9.6 million new cases being diagnosed each year.. DM may delay sputum conversion and may increase the case fatality rate during treatment. Aim of our study was to find out the clinical pattern, radiological pattern and response to treatment of pulmonary tuberculosis among patients with and without diabetes mellitus:
Materials and Methods: *150 diabetics and non-diabetics with sputum positive pulmonary tuberculosis were selected, as cases and controls respectively. Data regarding the socio-demographic profile, age, sex, clinical presentation and radiological pattern were collected. Sputum smear examination was done in all patient at diagnosis, end of IP and end of treatment. Treatment was considered to have failed if the patient is positive at the end of 5 months treatment.*
Results: *There was no significant difference in the symptomatology and symptom score between diabetics (2.77) and non-diabetics (2.14). A higher percentage of diabetics (18.8%) showed lower zone involvement when compared to non-diabetics (5.8%). 19.3% of the diabetics were sputum positive at the end of IP of which 4.4% were sputum positive at the end of 5 months and had to undergo a change in treatment regimen due to failure.*
Conclusion: *Tuberculosis and diabetes frequently coexist in our population. The presence of diabetes may not significantly influence the symptomatology of the patients. However, DM has a negative effect on TB treatment with a larger number of diabetics requiring a change in category of ATT.*
Keywords: *Pulmonary Tuberculosis, Diabetes Mellitus, Sputum Conversion.*

Introduction

Tuberculosis (TB) is one of the top 10 causes of death worldwide. In 2017, 10 million people fell ill with TB, and 1.6 million died from the disease (including 0.3 million among people with HIV). Globally, TB incidence is falling at about 2% per

year. This needs to accelerate to a 4–5% annual decline to reach the 2020 milestones of the End TB Strategy. An estimated 54 million lives were saved through TB diagnosis and treatment between 2000 and 2017. Ending the TB epidemic by 2030 is among the health targets of the Sustainable Development Goals(1). 425 million people have diabetes in the world and 82 million people in the South east Asian Region; by 2045 this will rise to 151 million. There were over 72,946,400 cases of diabetes in India in 2017(2). Persons with diabetes mellitus (DM) have a 3-fold increased risk of developing tuberculosis [3]. This increased risk has been ascribed to the intracellular nature of tuberculosis (TB) infection and impaired T-cell-mediated immune response in persons with DM[4]. Increasing rates of obesity and metabolic syndrome have led to an increasing prevalence of DM in many regions of the world. Many factors like Aging, changes in life style, socioeconomic factors, and population growth have lead to an increased prevalence of DM, particularly, type 2 DM. The total number of diabetic people worldwide is predicted to rise from 285 million in 2010, accounting for 3.5million deaths, to 439 million in 2030(5-7).Up to 80% of patients with DM comes from low socioeconomic group and developing countries.

17.5% of the world's population lives in India and is now undergoing rapid development and urbanisation. As a consequent there is increasing physical inactivity, an unhealthy diet and obesity which leads to an escalating epidemic of diabetes mellitus (DM)(8-10).

Response to anti-TB treatment has been reported to be slower and associated with worse outcomes in patients with DM and pulmonary TB. Delayed sputum smear and culture conversion after intensive phase of therapy[11,12] and increased treatment failure[13, 14], relapse, and death in patients with DM being treated for TB have been described; however, other studies found no differences in bacteriologic response and TB treatment outcomes comparing persons with and without DM[15,16]. The degree of dysglycemia may also affect treatment response. In a prospective hospital-based study from India, patients with pulmonary TB and DM with initial poor glycemic control had higher sputum smear grade, delayed smear conversion after 2 months of treatment, and higher treatment failure and relapse rates[17].

The objectives of our study are to evaluate the differences in clinical presentation and radiological pattern among patients with and without diabetes mellitus. And also to analyse the difference in response to treatment of pulmonary tuberculosis among patients with and without diabetes mellitus.

Methodology: Study design - A hospital based prospective study was conducted in department of respiratory medicine, Pariyaram medical college, Pariyaram for one year period. 150 diabetics and 150 non-diabetics with sputum positive pulmonary tuberculosis from our hospital and nearby tuberculosis units were selected for the study as cases and controls respectively. Patients with HIV and other immunosuppressive disorders were excluded from the study. Data regarding the socio-demographic profile, age, sex, clinical presentation and radiological pattern were collected. Radiological finding were grouped into normal, mild, moderate and severe

Mild--Sputum smear examination was done in all patient at diagnosis, end of IP and end of treatment. Additional smear examination was done when required. Treatment was considered to have failed if the patient is positive at the end of 5 months treatment. Data were entered into Microsoft EXCEL and analysed using SPSS.

Results

15 diabetics and 10 non diabetics were lost to follow up in the study. Hence total 275 (135 diabetics and 140 non-diabetics) patients were studied. 224(81.5%) were males. Most common age group affected was 50-59(33.5%). Fever was seen 225 patients. (119 diabetics and 106 non diabetics (p value 0.008)). Cough was present in 248 patients.(131 diabetics and117 non diabetics (p value<0.001)).

Breathlessness was present in 29 patients, 25 diabetics &4 non-diabetics which is statistically significant (p value<0.001). Night sweats was present in35 patients, 22 diabetics and 13 non diabetics (p value<0.081).There was no significant difference in symptom score between diabetics (2.77) and non-diabetics (2.14).

A higher percentage of diabetics (18.8%) showed lower zone involvement when compared to non-diabetics (5.8%) (p value<0.001). 19.3% of the diabetics were sputum positive at the end of IP of which 4.4% were sputum positive at the end of 5 months and had to undergo a change in treatment regimen due to failure. Only 1.4% of the non-diabetics failed to respond to treatment. The time to sputum conversion showed a more significant correlation with the initial bacillary load than with the diabetic status. There were Total 40 category 2 patients in which 22 were non-diabetic. Random blood glucose levels of diabetic patients ranged from 138 to 326 . All patients were treated with insulin during the course of ATT and all patients were in good glycemic control with insulin therapy.

Table-1 Percentage of patients with lower zone involvement in patients with diabetes and non diabetes

lower zone involvement * DIABETIC Cross tabulation					
			DIABETIC		Total
			YES	NO	
lower zone involvement	no	Count	54	98	152
		% within lower zone involvement	35.5	64.5	100.0
		% within DIABETIC	40.0	70.0	55.3
	yes	Count	81	42	123
		% within lower zone involvement	65.9	34.1	100.0
		% within DIABETIC	60.0	30.0	44.7
Total		Count	135	140	275
		% within lower zone involvement	49.1	50.9	100.0
		% within DIABETIC	100.0	100.0	100.0

p value-<0.0001

Table 2

sputumip_2 * DIABETIC Cross tabulation						
			DIABETIC		Total	
			YES	NO		p value
sputumip_2	negative	Count	109	119	228	
	positive	Count	26	21	47	0.348
Total		Count	135	140	275	

Table -3 Percentage of diabetics positive at end of extnded IP vs non diabetics

sputumextip_2 *DIABETIC Cross tabulation						
			DIABETIC		Total	
			YES	NO		p value
sputumextip_2	negative	Count	127	138	265	0.057
	positive	Count	8	2	10	
Total		Count	135	140	275	

Table-4 Percentage of diabetics positive at end of 5 months vs non diabetics

sputum5m_2 * DIABETIC Crosstabulation						
			DIABETIC		Total	
			YES	NO		p value
sputum5m_2	negative	Count	129	138	267	0.167
	positive	Count	6	2	8	
Total		Count	135	140	275	

Figure-1

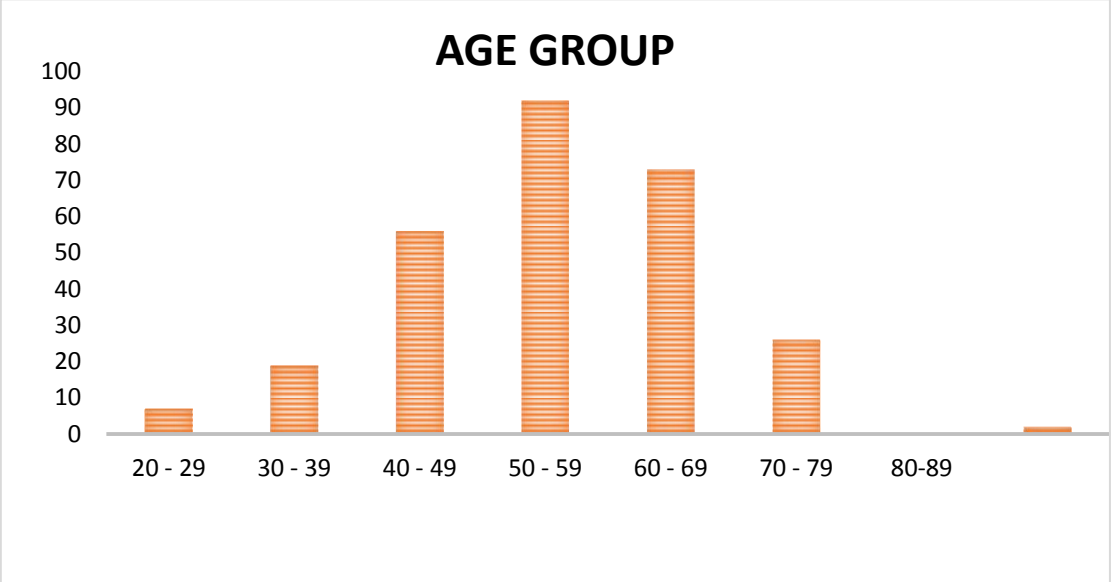


Figure-2

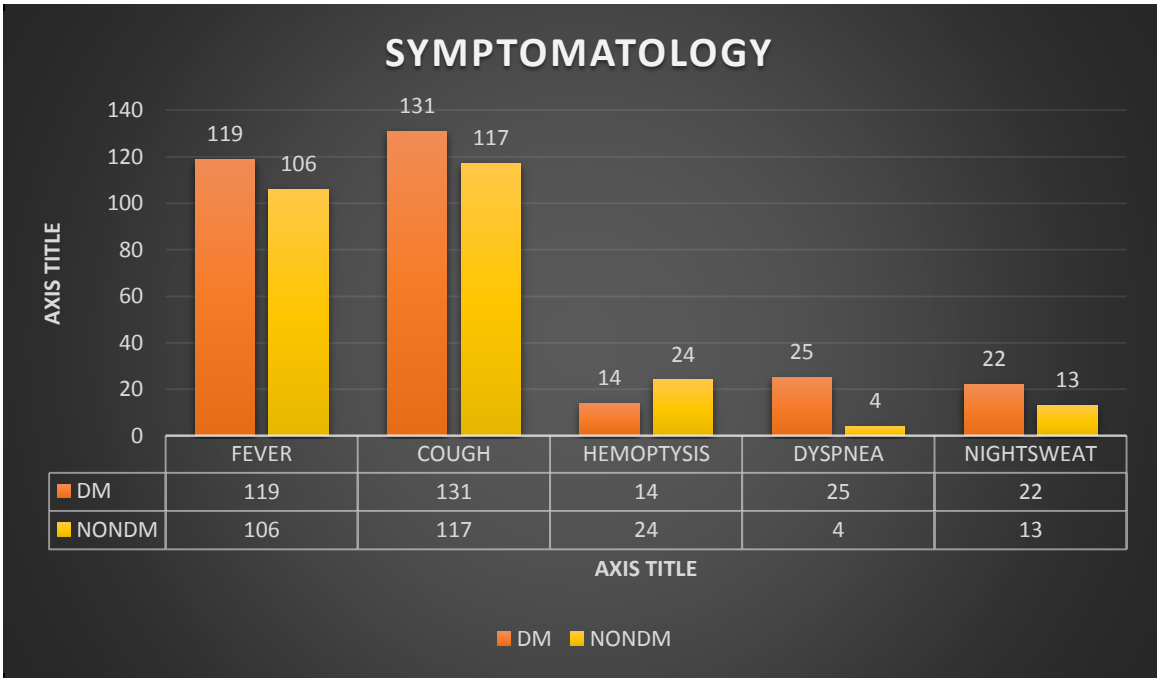


Figure-3

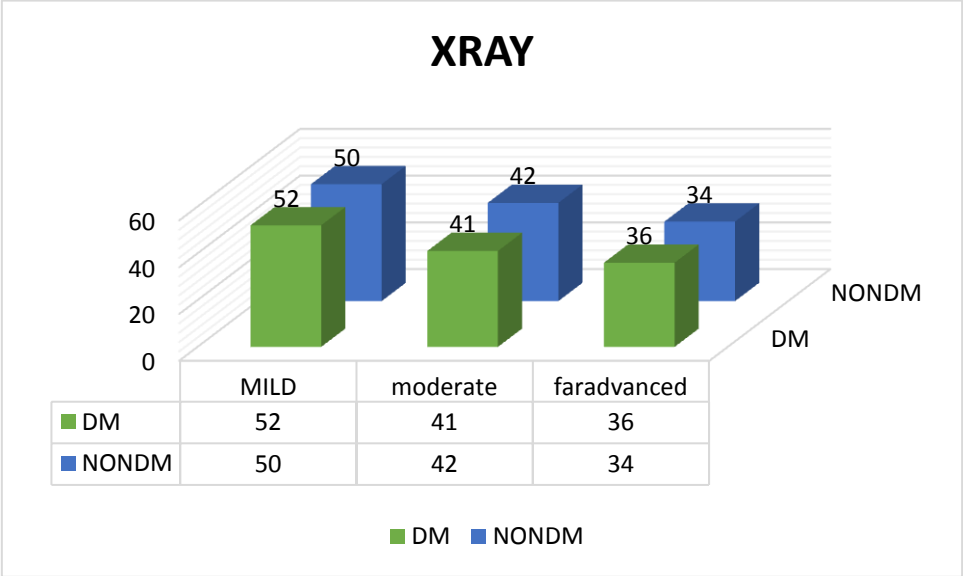
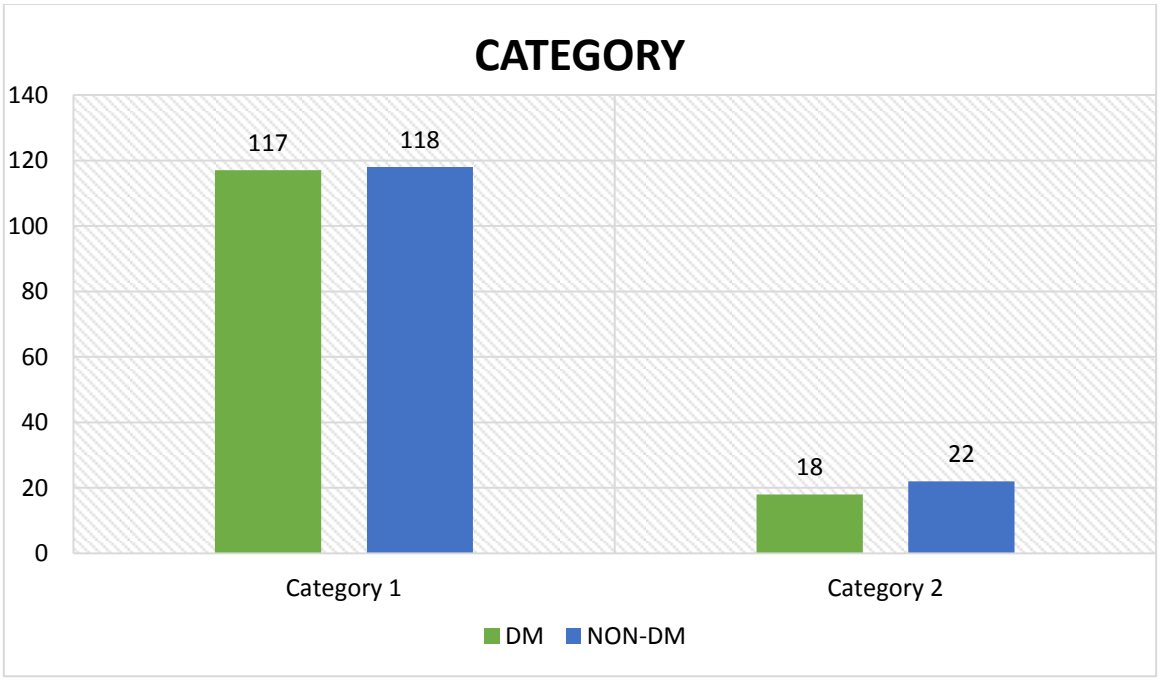


Figure-4 Category of TB



Discussion

Previous studies on the effect of DM on clinical, radiographic, and bacteriologic presentations of TB have suggested that patients with DM are more likely to present with atypical chest radiographic features, including more frequent lower lobe disease, fewer cavitary lesions, and diffuse lung involvement; however, reports have been inconsistent[18,19,20]. Our study shows a statistically significant lower lobe involvement in diabetics compared to non-diabetics. Two recent studies have shown that atypical chest radiographic findings and more severe radiographic disease were associated with higher hemoglobin A1c levels and poor chronic glycemic control among persons with DM and TB[21,22]. Present study included275 patients with sputum smear positive pulmonary tuberculosis-135 diabetic and 140 non diabetic. most common age group was 50-59. Present study showed more number of males in both groups. Study by Alisjahbana et al(23) did not show difference between two groups, and Study by Shingla et al(24) also showed more number of males than females.

Study done by Baby Nagapriya et al also showed a male predominance.[25].

Clinical profile: In our study Fever was seen 225 patients. 119 diabetics and 106 non diabetics (p value <0.008) but previous studies[24,25,26] showed no significant difference in two groups in symptoms at presentation.

Our study results were consistent with study by Alisjahbana et al[23], which showed more number of symptoms in patients with DM than in without DM,but conflicting with study done by Baby Nagapriya et al[25] which showed more number of symptoms in PTB patients without DM than in diabetic patients.

In Our study there was no significant difference in symptom score between diabetics (2.77) and non-diabetics (2.14). Study done by Baby nagapriya et al[25] showed a symptom score of (SS) of >4 was observed in 43.8% of patients with DM and 54.7% of PTB patients without DM. Alisjahbana et al (23) study showed SS>4 in 63.8% of patients with DM and 48.5% of PTB patients without DM.

Regarding the radiological findings: We have analyzed different radiological presentations in both groups and compared with each other and X-ray was graded into normal, mild, moderate and severe categories. In Our study Total 20 patients showed normal x ray chest, 14 non-diabetics &6 diabetics..

Mild X-ray finding at presentation in 102patients totally of which 52 patients were in DM group and 50patients were without DM. Severe in 36 of patients with DM and 34 of patients without DM. There is no difference in severe x-ray in two groups at presentation except slightly more in patients with DM. This is consistent with previous study[25]. Alisjahbana et al[23] study showed far advanced x-ray at presentation in 52.6% of patients with DM and 50.9% of patients without DM, which was not statistically significant. This finding also matches with our study.

Significant difference was there between two groups in our study in zone of involvement. Lower zone involvement is present in total 123 patients of which 81 patients were in DM group and 42 patients were without DM which is statistically significant (p value <0.0001).Study done by baby et al[25] also showed a lower zone involvement more in diabetics.. Study done by Shaikh MA et al[27], also showed PTB DM group of patients had increased frequency of lung lesions confined to lower lung field compared to PTB group DM. In our study total 47 patients were sputum AFB positive at the end of IP in which 26 were diabetics and 21 were non diabetics. More number of patients in our study still required intensive phase treatment at the end of 2 months when compared with patients without DM. This is consistent with previous study[25]. At the nd of extended IP 10 patients were AFB positive in which 8 were diabetics (p value0.057). At the end of 5 months total 8 patients were positive,6diabetics &2 non-diabetics.. Alisjahbana et al[23] study showed significant number of positive sputum culture results at the end of 6 months in DM group (22.2%), compared in patients without DM (9.6%) .

Conclusion

No significant difference in symptom presentation in both groups at presentation. Significant Lower zone involvement is observed in patients with DM. Slightly delayed sputum smear conversion rates at 2 months (at the end of intensive phase) in DM group though not significant statistically. Patients with DM required longer duration of intensive and continuation phase.

Limitations of Our Study

Radiological follow up not included in the study. Sputum culture for Tuberculosis and sensitivity testing (for MDR) was not included because of financial constraints.

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